SPARC Model Development/Enhancement for the Calculation of Molecular Descriptors and Reaction Rate Constants for Abiotic Transformations

Background Information

EPA's understanding of the chemical processes controlling the reduction and hydrolysis of chemicals containing reactive functional groups has grown significantly over the past 10 years. This includes the elucidation of transformation pathways, identification of molecular descriptors for QSAR (Quantitative Structure Activity Relationship) development and the identification of the dominant chemical reductants in anaerobic systems. In spite of this success, no models exist that allow for the estimation of reduction rates of chemicals with reducible functional groups in anaerobic systems. Also, the models for the estimation of hydrolysis rates are limited to carboxylic acid esters and epoxides.

In support of the Ecosystems Research Division (ERD) environmental fate research program, work is being conducted to (1) Enhance/develop SPARC calculators for the estimation of molecular descriptors required for the parameritization of QSARs for estimating reduction rate constants, (2) develop a SPARC calculator for reduction rates based on a model for electron transfer from surface complexed ferrous iron to the chemical of interest, and (3) extend the hydrolysis calculator to additional functional groups. Further details of this work are provided as follows:

ERD Research Task 1: Enhance/develop SPARC calculators for the parameritization of QSARs with molecular descriptors for estimating reduction rate constants

- **One-electron reduction potentials (E_1):**

One-electron reduction potentials have proven to be a very useful molecular descriptor for the reduction of halogenated aliphatics and nitroaromatic compounds (NACs) in reducing systems (see Tables 1 and 2 for a summary of the available computed E_1 values for halogenated aliphatics and NACs, respectively. The utility of E_1 for predicting reduction rates results from the observation that transfer of the first electron in NAC reduction to form the radical anion (i.e., ArNO2 + e- $\leftrightarrow$ ArNO2-•) represents the rate determining step in the reduction of NACs. In the absence of high quality measured data, however, the use of E_1 as a molecular descriptor remains limited due to the significant error typically associated with the calculation of this parameter. This error is attributed to the difficulties in predicting the energy of solvation for the radical anion formed in the electron transfer process.

- **Vertical Electron Affinity (VEA):**

VEA is the difference in energy between the neutral parent molecule and the corresponding anion that is formed by electron attachment without relaxation of the product (i.e., the equilibrium geometry of the neutral molecule). *VEA* values refer to the gas phase, and therefore, do not incorporate the effect of any changes in solvation.

Recently, a QSAR approach has been developed to calculate E_1 for NACs, based on *VEA*, its gas phase analogue (Phillips 2010). The *VEA* values used for the correlation were calculated using a scaled G3(MP2)//B3LYP method. The authors recommend caution in using the G3(MP2)//B3LYP method for the prediction of *VEA* values for ortho-substituted NACs due to the potential for strong interaction of the substituent with the nitro group.

- **Bond Dissociation Energies (DR-X):**

Electron transfer to halogenated organic compounds (R-X) is often concerted with cleavage of the R-X bond (i.e., $RX + e^- \rightarrow R\bullet + X^-$). QSARs based on calculated bond energies have been used successfully to predict reaction rates for the reduction of halogenated methanes and ethanes in reducing systems (e.g, Fe(II)/iron oxides and anaerobic sediments).

ERD Research Task 2: Enhance/develop SPARC calculators for estimating reaction rate constants for abiotic transformations

- **Abiotic reduction**

To date, kinetic studies for reductive transformations have focused primarily on model systems that are designed to mimic natural systems. The majority of these model systems have focused on Fe(II) in the presence of iron oxides. It is generally accepted that the active reductant in these systems is Fe(II) complexed at the iron hydroxide surface as illustrated below:


Surface Complexed Fe(II)
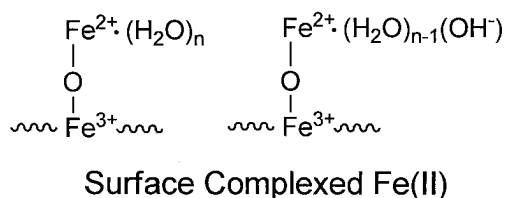
This figure illustrates both the protonated and deprotonated forms of the Fe(II) surface complex. Reactions rates for the reduction of NACs in Fe(II)/iron oxide systems increase with decreasing pH suggesting a greater contribution of electron density to Fe(II) through the OH⁻ group. It is generally assumed that electron transfer occurs through an outer sphere electron transfer process. Although natural reducing systems such as anaerobic sediment and aquifer are quite complex with respect to the potential chemical and biological reductants, studies of

NACs and halogenated methanes in anaerobic sediments support the scenario in which surface complexed Fe(II) is the dominant reductant for these chemicals.

- **Abiotic hydrolysis**

Hydrolysis is a chemical transformation process in which an organic compound, RX, reacts with water, forming a new carbon-oxygen bond and the cleaving of the carbon-X bond in the original molecule as shown in equation 1.

$$R\text{-}X \xrightarrow{\ H_2O\ } R\text{-}OH + X^- + H^+ \tag{1}$$
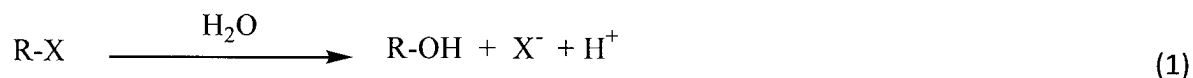
Hydrolysis reaction kinetics have been quantitatively modeled within the chemical equilibrium framework described in previous publications for ionization pK_a in water (Hilal, Carreira et al. 1994; Hilal, Brewer et al. 1995; Hilal and Karickhoff 1995; Hilal, Carreira et al. 1996; Hilal, Karickhoff et al. 1999). It is assumed that a reaction rate constant can be described in terms of the pseudo equilibrium constant between the reactant (initial) and transition (final) states of the molecule undergoing hydrolysis.

The hydrolysis models will be extended to halogenated alkanes. The models derived for estimating ester hydrolysis rate constants will be implemented directly in modeling new chemical classes. The SPARC models for the hydrolysis of amides will also be refined.

Contractor Statement of Work:

The contractor shall work in a consulting role with ERD staff to provide his/her expertise to accomplishing ERD Research Tasks 1 and 2 as described above. As required, the contractor will consult with ERD through participation in face-to-face meetings, teleconferences and email. Specific chemicals of interest are shown in the Figure.

Deliverables:

The contractor will provide quarterly progress reports including, but not limited, to the following information (beginning 3 months from contract award date):

Summary of the ongoing consultation with ERD staff concerning:

- the enhancement/development of SPARC calculators for the calculation of molecular descriptors required for the estimation of reduction and hydrolysis rate constants
  - o Provide a QA/QC analysis of the current SPARC calculator based on data sets provided by ERD staff
    - ■ Comparison of calculated vs. available measured and computed data

- Describe abilities and limitations of the current calculators(e.g., functional group or substructure limitations)
- Describe possible approaches and the necessary training data for overcoming these limitations

- Determining the feasibility of developing a SPARC calculator for calculating rates of reduction for nitroaromatics, N-nitrosamines, and halogenated aliphatics by surfaced-complexed Fe(II)
  - Determine feasibility based on available data provided by ERD staff
  - Describe possible approaches and the necessary training data for overcoming these limitations

Period of Performance: The period of performance shall be 12 months from the date of contract award. There are two additional option periods for 12 months each.

References:

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Totten, L. A. and A. L. Roberts (2001). "Calculated one- and two-electron reduction potentials and related molecular descriptors for reduction of alkyl and vinyl halides in water." Critical Reviews in Environmental Science and Technology 31(2): 175-221.

Table 1. One-Electron Reduction Potentials for Hydrogenolysis of Chlorinated Aliphatics

Name (Abbreviation)	Product	Scherer et al. [a] E_h^1 [b] or $E_h^{1'}$ [c] (V)	Totten et al. [d] $E_h^{1'}$ (V)	Cwiertny et al. [e] $E_h^{1'}$ (V)	Bylaska et al. [f] $E_h^{1'}$ (V)
Tetrachloro-methane (PCM)	$Cl_3C\bullet$	0.13 [b] (0.31)	0.085	0.182	-0.05
Trichloro-methane (TCM)	$HCl_2C\bullet$	-0.23 [b] (-0.053)	-0.145	-0.089	-0.314
Dichloro-methane (DCM)	$H_2ClC\bullet$	-0.50 [b] (-0.32)	-0.428	-0.323	-0.404
Chloro-methane (CM)	$H_3C\bullet$	-0.88 [b] (-0.70)	-0.725		-0.605
Hexachloro-ethane (HCA)	$Cl_3CCl_2C\bullet$	0.33 [b] (0.51)	0.061	0.144	0.265
Pentachloro-ethane (PCA)	$Cl_3CClHC\bullet$	0.00 [b] (0.18)	-0.132	-0.132	-0.161
Pentachloro-ethane (PCA)	$Cl_2HCCl_2C\bullet$	0.31 [b] (0.49)	0.139	0.092	0.079
1,1,1,2-Tetrachloro-ethane (1112TeCA)	$Cl_3CH_2C\bullet$	-0.52 [b] (-0.34)	-0.545	-0.413	-0.415
1,1,1,2-Tetrachloro-ethane (1112TeCA)	$ClH_2CCl_2C\bullet$	-0.22 [b] (-0.043)	0.044	0.046 [g]	0.046
1,1,2,2-Tetrachloro-ethane (1122TeCA)	$Cl_2HCClHC\bullet$	-0.34 [b] (-0.16)	-0.257	-0.132 [g]	-0.187
1,1,1-Trichloro-ethane (111TCA)	$H_3CCl_2C\bullet$	-0.23 [b] (-0.053)	-0.020	-0.046	-0.178
1,1,2-Trichloro-ethane (112TCA)	$Cl_2HCH_2C\bullet$	-0.74 [b] (-0.56)	-0.589		-0.497
1,1,2-Trichloro-ethane (112TCA)	$ClH_2CClHC\bullet$	-0.42 [b] (-0.24)	-0.285	-0.213 [g]	-0.264
1,1-Dichloro-ethane (11DCA)	$H_3CClHC\bullet$	-0.40 [b] (-0.22)	-0.316	-0.320	-0.439
1,2-Dichloro-ethane (12DCA)	$ClH_2CH_2C\bullet$	-0.57 [b] (-0.39)	-0.577	-0.426 [g]	-0.513
Chloroethane (CA)	$H_3CH_2C\bullet$	-0.83 [b] (-0.65)	-0.690		-0.646
Tetrachloroethene (PCE)	$Cl_2C=ClC\bullet$	-0.36 [c]	-0.598		-0.56
Trichloroethene (TCE)	$HClC=ClC\bullet$		-0.674		-0.838
Trichloroethene (TCE)	$Cl_2C=HC\bullet$	-0.91 [c]	-0.998		-0.998
Trichloroethene (TCE)	$ClHC=ClC\bullet$	-0.62 [c]	-0.693		-0.803
1,1-Dichloroethene (11DCE)	$H_2C=ClC\bullet$	-0.72 [c]	-0.802		-0.816
c-1,2-Dichloro-ethene (c12DCE)	$HClC=HC\bullet$	-0.89 [c]	-1.012		-0.959
t-1,2-Dichloro-ethene (t12DCE)	$HClC=HC\bullet$	-0.85 [c]	-0.955		-0.946
Chloroethene (VC)	$H_2C=HC\bullet$	-0.95 [c]	-1.141		-1.085

Name (Abbreviation)	Product	Scherer et al. [a] E_h^1 [b] or $E_h^{1'}$ [c] (V)	Totten et al. [d] $E_h^{1'}$ (V)	Cwiertny et al. [e] $E_h^{1'}$ (V)	Bylaska et al. [f] $E_h^{1'}$ (V)
1,1,1-Trichloro-propane (111TCP)	Cl$_2$C•-CH$_2$-CH$_3$				-0.192
1,1,2-Trichloro-propane (112TCP)	Cl$_2$HC-CH•-CH$_3$				-0.365
1,1,2-Trichloro-propane (112TCP)	ClHC•-CHCl-CH$_3$				-0.009
1,1,3-Trichloro-propane (113TCP)	Cl$_2$HC-CH$_2$-CH$_2$•				-0.608
1,1,3-Trichloro-propane (113TCP)	ClHC•-CH$_2$-CH$_2$Cl				-0.296
1,2,2-Trichloro-propane (122TCP)	ClH$_2$C-CCl•-CH$_3$				-0.157
1,2,2-Trichloro-propane (122TCP)	H$_2$C•-CCl$_2$-CH$_3$				-0.382
1,2,3-Trichloro-propane (TCP)	ClH$_2$C-CHCl-CH$_2$•				-0.491
1,2,3-Trichloro-propane (TCP)	ClH$_2$C-CH•-CH$_2$Cl				-0.443
1,1-Dichloro-propane (11DCP)	ClHC•-CH$_2$-CH$_3$				-0.439
1,2-Dichloro-propane (12DCP)	ClH$_2$C-CH•-CH$_3$				-0.595
1,2-Dichloro-propane (12DCP)	H$_2$C•-CHCl-CH$_3$				-0.63
1,3-Dichloro-propane (13DCP)	H$_2$C•-CH$_2$-CH$_2$Cl				-0.781
2,2-Dichloro-propane (22DCP)	H$_3$C-CCl•-CH$_3$				-0.634
1-Chloro-propane (1CP)	H$_2$C•-CH$_2$-CH$_3$				-0.66
2-Chloro-propane (2CP)	H$_3$C-CH•-CH$_3$				-0.699

[a] Dataset compiled in (Scherer, Balko et al. 1998) from E_h^1 data in (Curtis 1991) ([b]) and $E_h^{1'}$ data in (Roberts, Totten et al. 1996) ([c]); calculated $E_h^{1'}$ values from the original data in (Curtis 1991) shown in parenthesis. [d] From (Totten and Roberts 2001) for [Cl⁻] = 10⁻³ M. [e] From (Cwiertny, Arnold et al. 2010) for [Cl⁻] = 10⁻³ M. [f] Calculated from free energies reported in previous work by Bylaska et al., for chlorinated methanes (Bylaska, Dixon et al. 2002), ethenes (Bylaska, Dupuis et al. 2005; Bylaska, Dupuis et al. 2008), and propanes (Bylaska, Glaesemann et al. 2010). [g] Boltzmann average energy for all possible conformers (i.e., *syn* and *anti*).
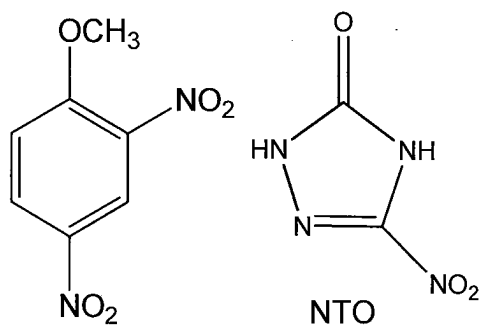
Table 2. One-Electron Reduction Potentials for Nitro Reduction

Name (Abbreviation)	Hoffstetter et al. [a] $E_h^{1'}$ (V)	Phillips, et al. [b] measured $E_h^{1'}$ (V)	Phillips et al. [c] corr. w/ EA $E_h^{1'}$ (V)	Zubatyuk et al. [d] E_h^1 (V)	Bylaska et al. $E_h^{1'}$ (V)
Nitrobenzene (NB)	-0.485	-0.486	-0.499	-0.88	-0.494
2-Methylnitro benzene (2-CH₃-NB)	-0.590	-0.590	-0.519		-0.612
3- Methylnitro benzene (3-CH₃-NB)	-0.475	-0.475	-0.507		-0.514
4- Methylnitro benzene (4-CH₃-NB)	-0.500	-0.500	-0.516		-0.538
2-Chloronitro benzene (2-Cl-NB)	-0.485		-0.470		-0.467
3-Chloronitro benzene (3-Cl-NB)	-0.405	-0.405	-0.437		-0.391
4-Chloronitro benzene (4-Cl-NB)	-0.450	-0.450	-0.447		-0.417
2-Acetylnitrobenzene (2-COCH₃-NB)	-0.470		-0.412		-0.445
3-Acetylnitrobenzene (3-COCH₃-NB)	-0.405	-0.437	-0.423		-0.406
4-Acetylnitrobenzene (4-COCH₃-NB)	-0.358	-0.356	-0.359		-0.255
2-4-6-Trinitro toluene (TNT)	-0.300	-0.253	-0.245	-0.45	
2-Amino-4,6-dinitro toluene (2-ADNT)	-0.390	-0.417	-0.386		
4-Amino-2,6-dinitro toluene (4-ADNT)	-0.430	-0.449	-0.393	-0.85	
2,4-Diamino-6-nitro toluene (2,4-DANT)	-0.515	-0.502	-0.557	-1.08	
2,6-Diamino-4-nitro toluene (2,6-DANT)	-0.495				
2,4-Dinitrotoluene (2,4-DNT)		-0.397	-0.361		
2,6-Dinitrotoluene (2,6-DNT)		-0.402	-0.377		
2-Nitroanaline (2-NH₂-NB)	< -0.560		-0.533		
3-Nitroanaline (3-NH₂-NB)	-0.500		-0.520		
4-Nitroanaline (4-NH₂-NB)		-0.568	-0.569		
1,2-Dinitrobenzene (1,2-DNB)		-0.287	-0.335	-0.50	
1,3-Dinitrobenzene (1,3-DNB)		-0.345	-0.330	-0.68	
1,4-Dinitrobenzene (1,4-DNB)		-0.257	-0.248	-0.43	
2-Nitrobenzaldehyde (2-CHO)		-0.355	-0.365		

4-Nitrobenzaldehyde (4-CHO)	-0.322	-0.330	-0.60
4-Nitrobenzyl alcohol (4-CH$_2$OH)	-0.478	-0.461	-0.90

[a] As reported and compiled in (Hofstetter, Heijman et al. 1999). [b] Measured values compiled by and reported in the supporting information of (Phillips, Sandler et al. 2011). [c] As reported in (Phillips, Sandler et al. 2011)—calculated from correlation with EA. [d] As reported in (Zubatyuk, Gorb et al. 2010).
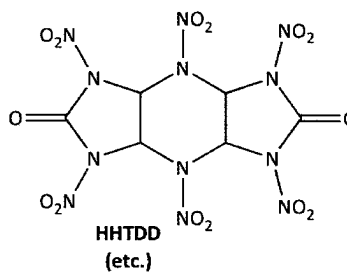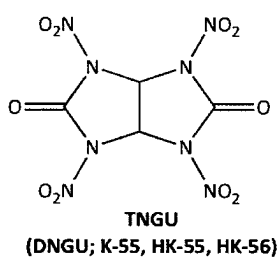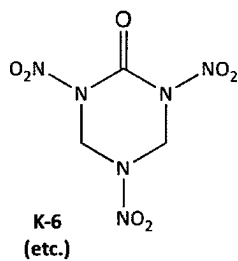
Specific Chemicals of Interest

NTO

Nitramines

TNAZ (etc.)

RDX (HMX, etc.)

CL-20 (TEX, etc.)

Nitroureas

K-6 (etc.)

TNGU (DNGU; K-55, HK-55, HK-56)

HHTDD (etc.)

Furoxans

CL-14 (ADNBF, etc.)

DDF (etc.)